



# Hepatitis B (Chronic, Acute, and Perinatal) and Hepatitis D

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## Disease Plan

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Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.



## CRITICAL CLINICAL INFORMATION

### Clinical Evidence

#### Signs/Symptoms

There are generally three phases of hepatitis B symptoms:

1. Pre-icteric or prodromal phase:
  - Nonspecific and usually presents with malaise, anorexia, nausea, vomiting, right upper quadrant abdominal pain, fever, headache, myalgia, skin rashes, arthralgia and arthritis, and dark urine. It generally lasts for 3–10 days.
2. Icteric Phase:
  - Occurs at the onset of jaundice, and is usually accompanied by light or gray stools, hepatic tenderness and hepatomegaly. This phase can last from 1–3 weeks.
3. Convalescent Phase:
  - Can last for weeks to months, and is characterized by malaise and fatigue.

#### Period of Communicability

- As long as HBsAg is detectable in the blood, person is considered infectious.
- An infected person can spread the virus to others starting a few weeks before symptoms appear and as long as they are infected.
- Chronically infected persons remain infectious for the rest of their lives.
- The period of time just prior to onset of acute illness is likely the most infectious period.

#### Incubation Period

- Range of 45-160 days, with an average of 90 days after exposure.

#### Mode of Transmission

- Blood or body fluids (semen, vaginal secretions, and saliva) via sexual contact, contact with contaminated blood, or perinatally.

### Laboratory Testing

Type of Lab Test	Also Known As	Type of Specimens	Collection Timing
Hepatitis B surface antigen	HBsAg	Blood/Serum, recalcified plasma, plasma	≥2 weeks after suspected exposure
Hepatitis B e antigen	HBeAg	Blood/Serum, recalcified plasma, plasma	≥2 weeks after suspected exposure
Nucleic acid test for hepatitis B DNA, including qualitative, quantitative, and genotype testing	HBV-DNA	Blood/Serum, recalcified plasma, plasma	≥2 weeks after suspected exposure
Hepatitis B core antigen IgM	Anti-HBc	Blood/Serum, recalcified plasma, plasma	≥2 weeks after suspected exposure
Hepatitis B Core Ab	Anti-HBc Ab	Blood/Serum, recalcified plasma, plasma	≥2 weeks after suspected exposure
Hepatitis B surface antibody	HBsAb	Blood/Serum, recalcified plasma, plasma	≥2 weeks after suspected exposure

### Treatment Recommendations

#### Type of Treatment

- For acute infection, no medication is available; treatment is supportive.
- There are several antiviral medications for persons with chronic infection. Persons with chronic HBV infection require linkage to care with regular monitoring to prevent liver damage and/or hepatocellular carcinoma.

**Time Period to Treat**

- As soon after exposure as possible

**Prophylaxis**

- Hepatitis B immune globulin (HBIG)
- Hepatitis B vaccine for those at risk of additional exposure
- For infants born to infected mothers, the combination of HBIG and vaccine is effective at preventing infection.

**Contact Management**

- Unvaccinated household members, syringe sharing partners, and sexual partners should initiate and complete post-exposure prophylaxis, which may include HBIG and/or hepatitis B vaccine according to age specifications. For additional post-exposure prophylaxis guidelines, see [https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a3.htm?s\\_cid=rr5516a3\\_e](https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a3.htm?s_cid=rr5516a3_e).
- Infants born to HBsAg-positive mothers should receive HBIG (0.5mL IM) and the first dose of hepatitis B vaccine within 12 hours of birth.
  - Infant should be screened for HBsAg and anti-HBs after completion of immunization series at 9–12 months of age.
  - If HBsAg is not present and anti-HBs antibody is  $\geq 10$  mIU/mL, children can be considered protected.
  - Infants with anti-HBs concentrations of  $< 10$  mIU/mL and who are HBsAg-negative should receive three additional doses of vaccine in a 0, 1, and 6-month schedule, followed by testing for anti-HBs 1–2 months after the sixth dose.
  - Infants who become HBsAg-positive despite immunization should be referred to a pediatric hepatologist for follow-up.
- Infants born to mothers whose HBsAg status is unknown should be given hepatitis B vaccine within 12 hours of birth, while awaiting HBsAg test results on the mother.
  - If mother is determined to be positive, the infant should receive HBIG as soon as possible, within seven days of birth. Infant should then complete the 3-dose hepatitis B vaccination series. The child should then be screened for HBsAg and anti-HBs at 9–12 months of age.
  - If mother is determined to be HBsAg-negative, the infant should complete the 3-dose hepatitis B vaccine series according to the schedule for infants born to HBsAg-negative mothers (0, 1–2, 6–18 months).
  - If mother's HBsAg status remains unknown, the infant should complete the vaccine series according to the recommended schedule for infants born to HBsAg-positive mothers (0, 1–2, 6 months). Administration of HBIG is not necessary.
- Infants that are  $< 12$  months of age and exposed after birth by primary caregivers with acute infection should receive HBIG (0.5mL IM) unless infant is fully immunized or has received at least two doses of vaccine.

**Isolation of Case**

- Those ill with acute HBV should stay home until fever and jaundice has resolved.

**Hospital**

N/A

**Quarantine**

N/A

**Infection Control Procedures**

- Vaccination
- Universal precautions
- Any blood spills, including dried blood, which can still be infectious, should be cleaned using 1:10 dilution of one part household bleach to 10 parts of water for disinfecting the area. Gloves should be used when cleaning up any blood spills.

## ✓ WHY ARE HEPATITIS B AND HEPATITIS D IMPORTANT TO PUBLIC HEALTH?

Hepatitis B is a liver infection caused by the hepatitis B virus (HBV). HBV is transmitted when blood, semen, or another body fluid from a person infected with HBV enters the body of someone who is not infected. This can happen through sexual contact; sharing needles, syringes, or other drug-injection equipment. In addition, infected mothers can transmit the infection to their infants at birth. For some people, HBV infection is an acute, or short-term, illness but for others, it can become a long-term, chronic infection. Risk for chronic infection is related to age: approximately 90% of infected infants become chronically infected compared with 2–6% of adults. Ongoing surveillance for acute HBV is needed to monitor and evaluate the effectiveness of current strategies for the control of disease and to identify exposed persons who will benefit from post-exposure prophylaxis.

An estimated 850,000 persons are living with HBV infection in the U.S. Persons with chronic HBV infection are a major reservoir for transmission of HBV infections. With widespread screening for HBV infection and the advent of laboratory reporting, an increasing number of persons testing positive for hepatitis B surface antigen (HBsAg) are being identified by state health departments. Chronic HBV carriers are at risk for infection with hepatitis D virus (HDV). HDV is an incomplete virus that requires the helper function of HBV to replicate. HDV infection of chronically infected HBV-carriers may lead to fulminant acute hepatitis or severe chronic active hepatitis, often progressing to cirrhosis. Surveillance data is needed to monitor the disease burden of chronic infection and to develop prevention programs.

## ✓ DISEASE AND EPIDEMIOLOGY

### Clinical Description

#### Hepatitis B infection

There are generally three phases of HBV symptoms.

- **Pre-icteric or prodromal phase**  
The pre-icteric or prodromal phase is nonspecific and usually presents with malaise, anorexia, nausea, vomiting, right upper quadrant abdominal pain, fever, headache, myalgia, skin rashes, arthralgia and arthritis, and dark urine. It generally lasts for 3–10 days.
- **Icteric Phase**  
The icteric phase occurs at the onset of jaundice, and is usually accompanied by light or gray stools, hepatic tenderness and hepatomegaly. This phase can last from 1–3 weeks.
- **Convalescent Phase**  
The convalescent phase can last for weeks to months, and is characterized by malaise and fatigue.

Severity of the disease ranges from unapparent cases (detectable only by liver function tests) to fulminant, fatal disease. Asymptomatic infections are common in children <5 years and among

immunocompromised adults, but can occur at any age. Among people  $\geq 5$  years, 30–50% will develop signs and symptoms.

### **Acute infection**

Once a person is infected with HBV, he/she will develop an acute infection. Symptoms may appear at this stage which can last for months. Persons with an acute infection can either make a complete recovery (which includes immunity to subsequent infection) or become chronic carriers. Most acute HBV infections in adults result in complete recovery with elimination of HBsAg from the blood and the production of anti-hepatitis B surface antibody (anti-HBs), creating immunity to future infection.

### **Chronic infection**

Overall, approximately 5% of all acute HBV infections progress to chronic infection, with the risk of chronic HBV infection decreasing with age. As many as 90% of infants who acquire HBV infection from their mothers at birth become chronically infected. Of children who become infected with HBV between one year and five years of age, 30–50% become chronically infected. By adulthood, the risk of acquiring chronic HBV infection is approximately 2–6%. Persons with chronic infection are often asymptomatic and may not be aware that they are infected; however, they are capable of infecting others and are termed “carriers.”

Most persons acutely infected completely recover from the disease with no complications. However, 1–2% may develop fulminant hepatitis. The majority of complications occur with chronic infection. Chronic infection may result in chronic hepatitis, cirrhosis, liver failure, and hepatocellular carcinoma. Approximately 25% of persons with chronic HBV infection die prematurely from cirrhosis or liver cancer. Chronic active hepatitis develops in more than 25% of carriers and often results in cirrhosis.

### **Perinatal infection**

Perinatal transmission from mother to infant at birth is very efficient. If the mother is positive for both HBsAg and hepatitis e-antigen (HBeAg), 70%–90% of infants will become infected in the absence of post-exposure prophylaxis. The risk of perinatal transmission is about 10% if the mother is positive only for HBsAg. Infants infected with HBV have a 90% chance of becoming chronic carriers.

### **Hepatitis D co-infection**

An HDV co-infection occurs when a patient infected with HBV is infected with HDV. The onset of acute co-infection is typically abrupt and resembles the signs and symptoms of acute HBV infection, including anorexia, abdominal pain, nausea, vomiting, and jaundice. Although co-infection usually results in self-limited disease, the likelihood of fulminant hepatitis is higher with coinfection and can be as high as 5%. Like HBV infections, HDV infections can also be acute or chronic. Progression to cirrhosis is believed to be more common with HBV-HDV chronic infections.

### **Causative Agent**

HBV infection is caused by the hepatitis B virus, a double-stranded DNA virus in the family Hepadnaviridae. Important components of the viral particle include hepatitis B surface antigen (HBsAg), hepatitis B core antigen (HBcAg), and hepatitis B e antigen (HBeAg).

HDV is a single-stranded RNA virus that contains hepatitis B surface antigen (HBsAg) within its coat. HDV requires the HBV as a “helper” virus, and it cannot produce infection in the absence of HBV infection. It is in the same viral family as HBV.

## **Differential Diagnosis**

Hepatitis has a variety of causes including, but not limited to: viral hepatitises (A, B, C, D, E, X), Epstein-Barr virus, cytomegalovirus, drug-induced hepatitis, toxin-induced hepatitis, auto-immune hepatitis, and alcohol liver disease.

## **Laboratory Identification**

### **Hepatitis B**

HBV infection cannot be definitively diagnosed without a blood test that measures various serologic markers for hepatitis B virus.

### **Serology panels**

Infection with HBV is associated with characteristic changes in the serum levels of HBV antigens and antibodies. These markers are used to define different clinical states.

### **Hepatitis B surface antigen and antibody**

Hepatitis B surface antigen (HBsAg) is the serologic hallmark of HBV infection. It can be detected by radioimmunoassays (RIA) or enzyme immunoassays (EIA).

HBsAg appears in serum 1 to 10 weeks after an acute exposure to HBV, prior to the onset of hepatitic symptoms or elevation of serum alanine aminotransferase (ALT) (Figure 1). In patients who subsequently recover, HBsAg usually becomes undetectable after four to six months. Persistence of HBsAg for more than six months implies chronic infection. It is estimated that less than 1% of immunocompetent adult patients with genuine acute HBV infection progress to chronic infection. Among patients with chronic HBV infection, the rate of clearance of HBsAg is approximately 0.5% per year.

The disappearance of HBsAg is followed by the appearance of hepatitis B surface antibody (anti-HBs). In most patients, anti-HBs persist for life, thereby, conferring long-term immunity. In some patients, however, anti-HBs may not be detectable until after a window period of several weeks to months, during which neither HBsAg nor anti-HBs can be detected. At this time, the serologic diagnosis may be made by the detection of IgM antibodies against hepatitis B core antigen (IgM anti-HBc).

HBV can be classified into at least eight genotypes and four major serotypes. All HBV serotypes share one common antigenic determinant: “a.” The “a” determinant of HBV is the most important target for diagnosis and immunoprophylaxis. Antibodies to the “a” determinant confer protection to all HBV serotypes.

Paradoxical coexistence of HBsAg and anti-HBs has been reported in approximately 24% of HBsAg positive individuals. In most instances, the antibodies are unable to neutralize the circulating virions. These individuals should therefore be regarded as carriers of HBV.

### **Hepatitis B core antigen and antibody**

Hepatitis B core antigen (HBcAg) is an intracellular antigen that is expressed in infected hepatocytes. It is not detectable in serum. Anti-HBc can be detected throughout the course of HBV infection (Figure 1).

During acute infection, anti-HBc is predominantly of IgM class. IgM anti-HBc is the sole marker of HBV infection during the window period between the disappearance of HBsAg and the appearance of anti-HBs. The detection of IgM anti-HBc is usually regarded as an indication of acute HBV infection.

However, IgM anti-HBc may remain detectable up to two years after the acute infection. Furthermore, the titer of IgM anti-HBc may increase to detectable levels during exacerbations of chronic HBV infection. This can present a diagnostic problem, incorrectly suggesting acute HBV infection, particularly in endemic areas in which many HBsAg-positive patients presenting with acute hepatitis actually have exacerbations of chronic HBV infection. Other common causes of acute exacerbation of chronic HBV infection are superinfected with HDV or hepatitis C virus (HCV).

Anti-HBc persists along with anti-HBs in patients who recover from acute HBV infection. It also persists in association with HBsAg in those who progress to chronic HBV infection.

### **Isolated anti-HBc**

The isolated presence of anti-HBc in the absence of HBsAg and anti-HBs has been reported in 0.4–1.7% of blood donors in low prevalence areas and in 10–20% of the population in endemic countries. Isolated detection of anti-HBc can occur in three settings: during the window period of acute HBV infection when the anti-HBc is predominantly IgM class; many years after recovery from acute HBV infection when anti-HBs has fallen to undetectable levels; and after many years of chronic HBV infection when the HBsAg titer has decreased below the cutoff level for detection. As noted above, loss of detectable HBsAg occurs in approximately 0.5% of patients with chronic HBV per year.

The clinical significance of isolated anti-HBc is unclear. Although HBV-DNA has been detected in the serum of individuals with isolated anti-HBc when tested by PCR assays, the frequency of detection varies from 0–20%. HBV-DNA can be detected in the liver of most (more than 70%) persons with isolated anti-HBc. Transmission of HBV infection has been reported from blood and organ donors with isolated anti-HBc, but the incidence ranged widely from 0.4–78 %. The risk is highest when liver from anti-HBc positive donors are transplanted.

Studies in the late 1980s suggest that (based upon the development of a primary anti-HBs response to HBV vaccination of asymptomatic individuals with isolated anti-HBc) as many as 50–80% of persons with isolated anti-HBc have false positive test results. Nonspecific results appear to be more common with anti-HBc enzyme immunoassays than with radioimmunoassays. However, improvement of enzyme immunoassays in the past decade has decreased the rate of false positive results.

The evaluation of individuals with isolated anti-HBc should include repeat testing for anti-HBc, HBsAg, anti-HBe, and anti-HBs. In addition:

- Among patients who remain positive for isolated anti-HBc IgG, those with evidence of a recent HBV exposure, symptoms of acute hepatitis, and/or markedly elevated ALT levels should be tested for the presence of anti-HBc IgM to rule out recent HBV infection.
- Individuals with evidence of chronic liver disease should be tested for HBV-DNA to exclude low level chronic HBV infection.

### **Hepatitis B e antigen and antibody**

Hepatitis B e antigen (HBeAg) is a secretory protein that is processed from the pre-core protein. It is generally considered to be a marker of HBV replication and infectivity. The presence of HBeAg is usually associated with high levels of HBV DNA in serum and higher rates of transmission of HBV infection from carrier mothers to their babies and from patients to healthcare workers.

HBeAg to anti-HBe seroconversion occurs early in patients with acute infection, prior to HBsAg to anti-HBs seroconversion (Figure 1). However, HBeAg seroconversion may be delayed for years to decades in patients with chronic HBV infection. In such patients, the presence of HBeAg is usually associated with the detection of high levels of HBV DNA in serum and active liver disease. However, HBeAg-positive patients with perinatally acquired HBV infection may have normal serum ALT concentrations and minimal inflammation in the liver.

Seroconversion from HBeAg to anti-HBe is usually associated with a decrease in serum HBV DNA and remission of liver disease. However, some patients continue to have active liver disease after HBeAg seroconversion. Such individuals may have low levels of wild type HBV or HBV variants with a stop codon in the pre-core or dual nucleotide substitutions in the core promoter region that prevent or decrease the production of HBeAg.

### **Serum HBV-DNA assays**

Qualitative and quantitative tests for HBV-DNA in serum have been developed to assess HBV replication. The sensitivity limit of these assays depends upon the techniques used.

Recovery from acute HBV infection is usually accompanied by the disappearance of HBV-DNA in serum as determined by hybridization or bDNA assays. However, HBV-DNA may remain detectable in serum for many years if tested by PCR assays. This observation suggests that the virus persists after "recovery," but is controlled by the immune system.

HBV-DNA levels are also detectable in patients with HBeAg negative chronic hepatitis, although levels are generally lower than in patients with HBeAg positive chronic hepatitis.

Several serologic tests are needed to determine the status of the patient's immunity and/or infection. The three most commonly ordered tests that make up the basic HBV testing panel are HBsAg, anti-HBc, and anti-HBs. The following table displays serologic test interpretations.

Refer to the table below for serologic tests available and what their results usually mean.



**Table 1. Antibody and antigen biomarkers for hepatitis B infection**

Clinical state	HBsAG	Total anti-HBs	Total anti-HBc	Action
Chronic infection	Positive	Negative	Positive	Link to hepatitis B-directed care
Acute	Positive	Negative	Positive (IgM anti-HBc)	Link to hepatitis B-directed care
Resolved infection	Negative	Positive	Positive	Counseling, reassurance
Immune (immunization)	Negative	Positive	Negative	Reassurance
Susceptible (never infected and no evidence of immunization)	Negative	Negative	Negative	Vaccinate
*Isolated core antibody	Negative	Negative	Positive	Depends on situation

Notes:

\*can be a result of:

<sup>1</sup>False positive: Repeat testing required

<sup>2</sup>Past infection: No action needed

<sup>3</sup>Occult HBV infection: Needs to be known if patient ever becomes immunosuppressed or given chemotherapy or treated with antiviral therapy for hepatitis C virus infection. Consider monitoring HBV-DNA.

<sup>4</sup>Passive transfer to infant born to HBsAg-positive mother No specific action needed.

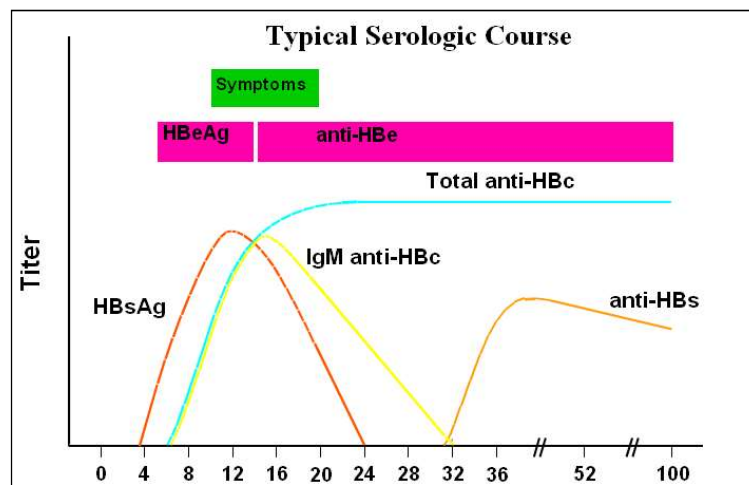
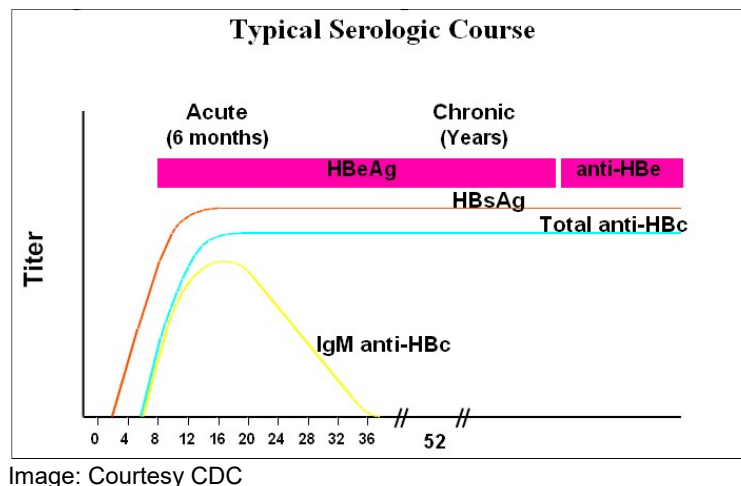
**Figure 1. Acute hepatitis B virus infection with recovery**


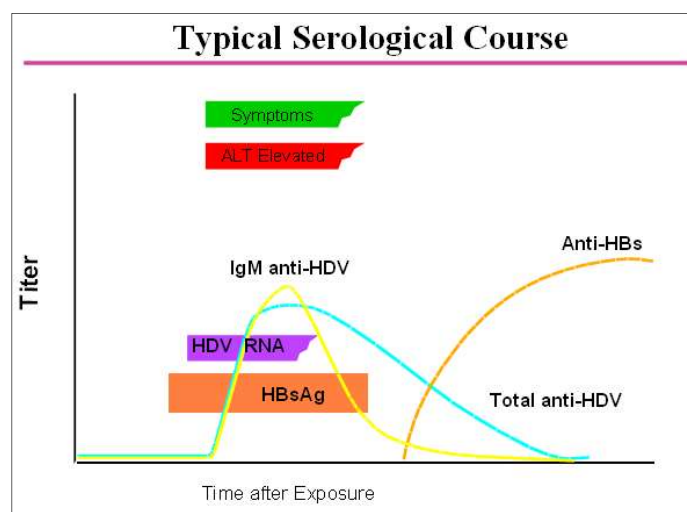
Image: Courtesy CDC

**Figure 2. Progression to chronic hepatitis B virus infection**


### Hepatitis D

Laboratory tests for HDV include IgM anti-HDV, IgG anti-HDV, HDAg, and HDAb (anti-HDV). A person infected with HDV will always be IgM anti-HDV positive. However, for a co-infection, they will also be IgM anti-HBV positive, whereas, for a super-infection, they will be IgM anti-HBV negative.

In about 15% of patients the only evidence of HDV infection may be the detection of either IgM anti-HDV alone during the early acute period of illness or IgG anti-HDV alone during convalescence. Anti-HDV generally declines to sub-detectable levels after the infection resolves, and there is no serologic marker that persists to indicate that the patient was ever infected with HDV. HDAg can be detected in serum in only about 25% of patients with HBV-HDV co-infection. When HDAg is detectable, it generally disappears as HBsAg disappears, and most patients do not develop chronic infection. Tests for IgG anti-HDV are commercially available in the U.S.

**Figure 3. HBV-HCV co-infection**


In patients with chronic HBV infection who are super-infected with HDV, several characteristic serologic features generally occur, including: 1) the titer of HBsAg declines at the time HDAg appears in the serum, 2) HDAg and HDV RNA remain detectable in the serum because chronic HDV infection generally occurs in most patients with HDV superinfection, unlike the case with co-infection, 3) high titers of both IgM and IgG anti-HDV are detectable, which persist indefinitely.

**Figure 4. HBV-HDV super-infection**

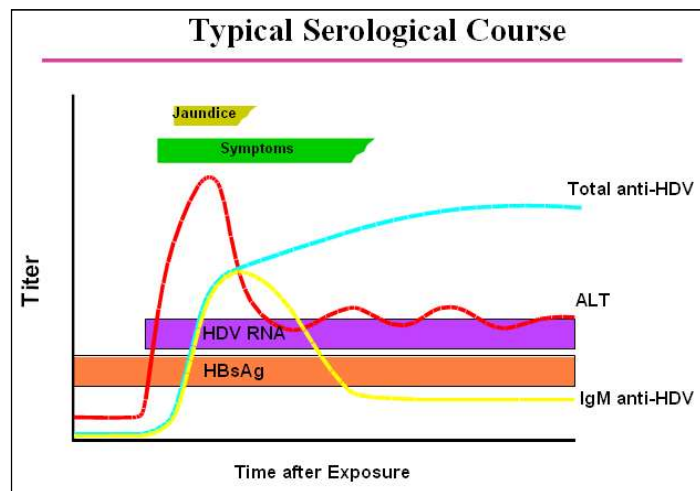


Image: Courtesy CDC

### Chemistry panels

Liver function tests, such as ALT and AST (aminotransferases) are sensitive for liver damage, but are not specific for HBV. In patients without jaundice, elevated serum aminotransferase levels are required to meet the clinical case definition. The normal value for ALT and AST is up to 50 mIU/mL, but reference ranges can be laboratory specific, so, it is appropriate to ask the laboratory performing this test to provide their reference range.

### Utah Public Health Laboratory (UPHL)

The UPHL performs HBsAg (including confirmatory testing), and anti-HBs testing. Testing is performed twice a week, once on Monday and Thursday.

### Treatment

Treatment for acute HBV and HDV is mainly supportive. In recent years, there have been an increasing number of antiviral treatment options for chronic HBV and HDV.

- **Interferon:** The advantages of interferon compared to the other options are its finite duration of treatment, the absence of selection of resistant mutants, and a more durable response. On the other hand, side effects from interferon are troubling for many patients, and (less commonly) can be severe. Furthermore, interferon cannot be used in patients with decompensated disease. The main role of interferon is primarily treatment of young patients with well compensated liver disease who do not wish to be on long-term treatment or are planning to be pregnant within the next two to three years. Interferon is also an attractive option for patients with HBV genotype A infection. Interferon is the most effective treatment for chronic HBV and HDV carriers and is successful in 25–50% of cases.

- Dosing recommendations:
  - For adults: 5 MU daily or 10 MU three times per week.
  - For children: 6 MU/M(2) three times weekly with a maximum of 10 MU.
  - Treatment duration for HBeAg positive chronic hepatitis is 16 to 32 weeks.
  - Treatment duration for HBeAg negative hepatitis is 12 to 24 months.
- **Lamivudine:** The main advantages of [lamivudine](#) are its lower cost compared to the other oral agents and the many years of experience confirming its safety, including its use during pregnancy. Compared to [adefovir](#), lamivudine has more rapid and more potent virus suppression, but [entecavir](#), [telbivudine](#), and tenofovir are superior to lamivudine in suppressing viral replication. The main disadvantage of lamivudine is the high rate of drug resistance. The role of lamivudine in the care of HBV is diminishing with the availability of new therapies which are associated with lower rates of drug resistance. Lamivudine may still have a role in patients co-infected with HIV (in whom lamivudine may be part of the antiretroviral regimen which contains a second drug with anti-HBV activity such as tenofovir).
  - Dosing recommendations:
    - The recommended dose for adults with normal renal function without concomitant HIV infection is 100 mg daily. Dose adjustment is required in those with decreased renal function.
    - The recommended dose for children is 3 mg/kg per day with a maximum of 100 mg/day.
    - The recommended dose for those who are co-infected with HIV is 150 mg twice daily (along with other anti-retroviral drugs).
- **Adefovir:** The main advantage of adefovir is its activity against lamivudine-resistant HBV and a lower rate of drug resistance compared to lamivudine. However, virus suppression is slow at the approved dose and up to 25% of patients experience minimal or no viral suppression. Adefovir at high doses has been associated with nephrotoxicity. At the approved dose of 10 mg daily, reversible increase in serum creatinine has been reported in 3n9% of patients after four to five years of treatment. Adefovir resistance was not detected after one year of treatment but the rate of drug resistance has been reported to be as high as 29% after five years of treatment. The most important role of adefovir is in the treatment of patients with lamivudine-resistant HBV, preferably in combination. With the approval of tenofovir, which is more potent, the role of adefovir is rapidly diminishing.
  - Dosing recommendations:
    - Adefovir is administered orally. The dose is 10 mg daily. Patients with impaired renal function should have the dosing interval adjusted.
- **Entecavir:** The main advantages of entecavir are its potent antiviral activity and a low rate of drug resistance. Entecavir has a more important role in primary treatment of HBV than in patients with lamivudine-resistant HBV. Entecavir may also have an important role in patients with decompensated cirrhosis because of its potent antiviral activity and low rate of drug resistance.
  - Dosing recommendations:
    - Entecavir is administered orally. The recommended dose is 0.5 mg once daily for nucleoside-naïve adults and adolescents older than 16 years of age, while it is 1 mg daily for those who have lamivudine resistance and those with

decompensated liver disease. The dose should be adjusted in patients with a creatinine clearance of <50 mL/min.

- **Telbivudine:** Telbivudine appears to have slightly more potent antiviral effects compared with lamivudine and adefovir, but it selects for the same resistant mutants as lamivudine and is more expensive. Thus, its role as primary therapy is limited. Furthermore, there have been rare cases of myopathy and peripheral neuropathy.
  - Dosing recommendations:
    - Telbivudine is administered orally. The recommended dose is 600 mg once daily.
- **Tenofovir:** Tenofovir is used as first-line therapy for treatment-naïve patients and for most patients with drug-resistant virus. Resistance to tenofovir is unlikely to develop, even among patients who have been treated for up to eight years. Tenofovir is effective in suppressing wild-type as well as lamivudine, telbivudine, or entecavir-resistant HBV. It is also effective in suppressing adefovir-resistant HBV, although the efficacy is lower in patients with double mutations.
  - Dosing recommendations:
    - Tenofovir is given at a dose of 300 mg daily; the dose needs to be adjusted in renal impairment.

The rationale for treatment in patients with chronic HBV is to reduce the risk of progressive chronic liver disease, transmission to others, and other long-term complications from chronic HBV such as cirrhosis and hepatocellular carcinoma. The optimal treatment of HDV is uncertain. Thus, patients should ideally be treated as part of a clinical trial. The only treatment approved for chronic HDV is interferon. The aim of treatment of HDV is to eradicate or to achieve long-term suppression of both HDV and HBV.

## Case Fatality

The World Health Organization (WHO) estimates that more than 2 billion persons have been infected with HBV globally (including 240 million chronically infected). An estimated 5% of the 240 million people infected with HBV globally have serologic evidence of exposure to HDV. Each year approximately 600,000 persons die as a result of HBV infection. The case-fatality rate in hospitalized patients is about 1%. Disease tends to be worse and mortality higher in those over 40 years of age.

## Reservoir

Humans are the only natural host for HBV and HDV. Chimpanzees are susceptible, but an animal reservoir in nature has not been recognized. Closely related hepadnaviruses are found in woodchucks, squirrels, and other animals, such as snow leopards and German herons; none cause disease in humans.

## **Transmission**

### **Hepatitis B**

HBV is transmitted through blood or body fluids, including wound exudates, semen, vaginal secretions, and saliva. Blood and serum contain the highest concentrations of the virus; saliva contains the lowest. Common modes of transmission include sexual contact, contact with contaminated blood, or perinatally – from a mother to child at birth. Contact with contaminated blood can occur through needle sticks, sharing or reusing non-sterile needles or syringes, transfusion of blood and blood products (rare in the U.S. due to current blood donor screening and testing protocols), hemodialysis, and tattooing.

Person-to-person spread of HBV can occur in settings involving interpersonal contact over extended periods, such as when a chronically infected person resides in a household. In household settings, nonsexual transmission occurs primarily from child to child, and young children are at highest risk for infection. The precise mechanisms of transmission from child to child are unknown; however, frequent interpersonal contact of non-intact skin or mucous membranes with blood-containing secretions or saliva are the most likely means of transmission. HBV can survive outside the body for at least seven days. During this time, the virus can still cause infection if it enters the body of a person who is not protected by the vaccine. Sharing of personal items such as washcloths, towels, razors, or toothbrushes, are behaviors that can facilitate transmission. Fecal-oral transmission does not appear to occur. Approximately one-third of infected persons do not have a readily identifiable risk factor.

### **Hepatitis D**

HDV can be transmitted through blood or blood products, injection drug use, or sexual contact, as long as HBV is also present in the patient.

## **Susceptibility**

Once infected with HBV, a person cannot get the disease again. However, HBV infection does not protect against other types of hepatitis. HDV can be transmitted only if HBV is also present in the patient.

## **Incubation Period**

### **Hepatitis B**

Symptoms of HBV develop slowly and on average appear 90 days after exposure, with a range of 45–160 days. The likelihood of developing symptoms of acute hepatitis is age dependent: less than 1% of infants younger than 1 year, 5–15% of children 1 through 5 years of age, and 30–50% of people older than five years of age are symptomatic, although few data are available for adults older than 30 years of age.

### **Hepatitis D**

The incubation period for HDV super-infection is about 2–8 weeks. With acute co-infection of HBV and HDV, the incubation period is similar to that of HBV (45–160 days; average, 90 days).

## Period of Communicability

A person with HBV infection is considered infectious as long as HBsAg is detectable in the blood. An infected person can spread the virus to others starting a few weeks before symptoms appear and as long as they are infected. Persons chronically infected remain infectious for the rest of their lives. HDV is likely transmissible during all phases of infection. The period of time just prior to the onset of acute illness is likely the most infectious period.

## Epidemiology

### Hepatitis B

Worldwide, HBV is a major cause of chronic liver disease and liver cancer. The frequency of HBV infection and patterns of transmission vary greatly throughout the world. Approximately 45% of people worldwide live in regions of high HBV endemicity, where the prevalence of chronic HBV infection is 8% or greater. Historically in these regions, most new infections occurred as a result of perinatal or early childhood infections.

**Figure 5. Worldwide rates of chronic hepatitis B**

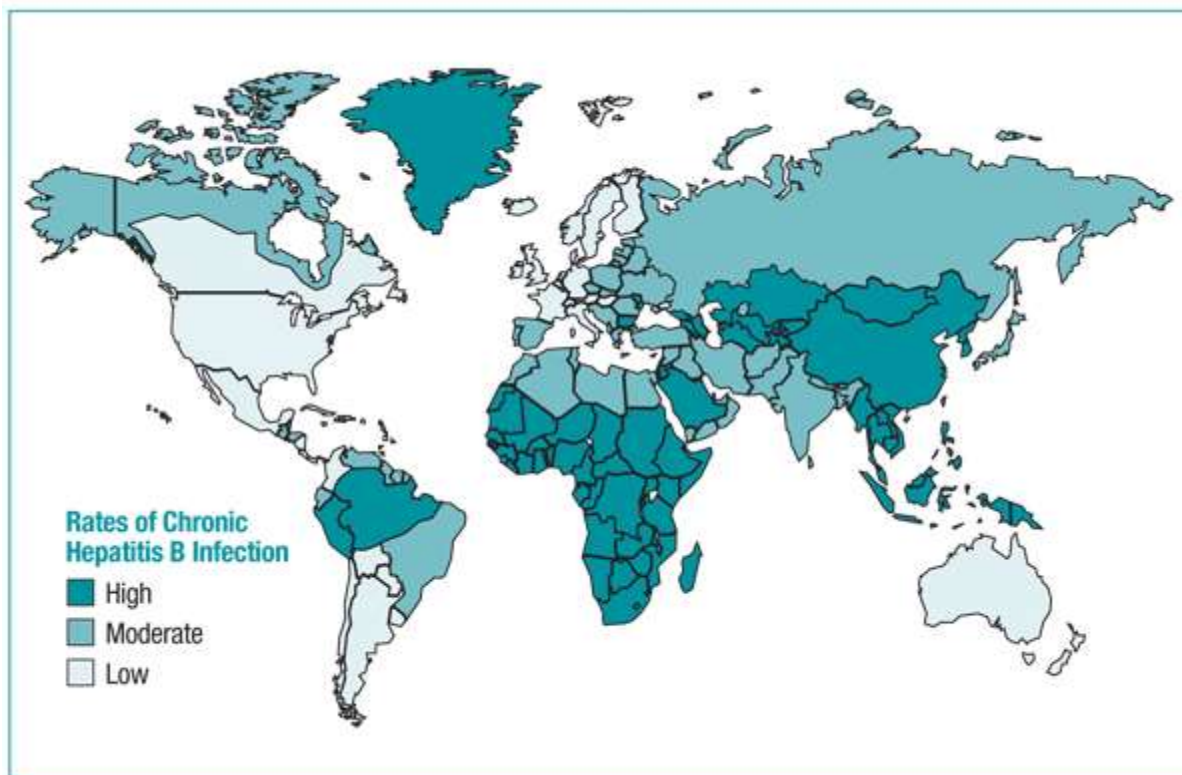


Image: Courtesy CDC (2014)

Acute HBV infection is reported most commonly among adults 30 through 49 years of age in the U.S. Since 1990, the incidence of acute HBV infection has declined in all age categories, with a 98% decline in children younger than 19 years, and a 93% decline in young adults 20 through 29 years of age, with most of the decline among people 20 through 24 years of age. Perinatal transmission in the U.S. is low because of high coverage with the HBV vaccine and immunoglobulin of infants born to chronically infected mothers at birth. In addition, since 1982 when HBV vaccine

first became available, the Advisory Committee on Immunization Practices (ACIP) has gradually evolved recommendations toward universal vaccination of infants as part of a comprehensive strategy to eliminate HBV transmission.

Within the U.S., there are pockets of high endemicity, including first-generation immigrants from areas where HBV is endemic, Alaskan Natives, and some inner city populations. The highest risk of early childhood infection is among children born to mothers from HBV endemic countries.

Other persons at risk of infection include:

- Household contacts of people with chronic HBV infection
- Residents of institutions for the developmentally disabled
- Patients undergoing hemodialysis
- Patients with clotting disorders and others repeatedly receiving blood products.

In the U.S., the most common risk factors for HBV infection are injection drug use, people with multiple heterosexual partners, men who have sex with men, and people who reported surgery during the six weeks to six months prior to onset of symptoms, respectively. Acute HBV infection occurs most commonly among adolescents and adults.

Groups at highest risk include:

- Men who have sex with other men
- Heterosexuals with multiple sex partners
- Persons diagnosed with a recently acquired sexually transmitted disease
- Prostitutes
- Injection-drug users who share needles
- Inmates of long-term correctional facilities
- Persons undergoing hemodialysis
- Healthcare workers (depends on how often they are exposed to blood or blood products through percutaneous and permucosal exposures).

## **Hepatitis D**

An estimated 18 million people worldwide are co-infected with HDV and HBV. In the U.S., the incidence of HDV cannot be directly calculated from national surveillance data because HDV is not currently nationally reportable. However, in prevalence studies among patients with acute HBV infection, 1.5–7.2% had serologic evidence of HBV-HDV co-infection.

In general, the global pattern of HDV infection corresponds to the prevalence of chronic HBV infection; however, several distinct features of the distribution of HDV infection have been identified. In countries with a low prevalence of chronic HBV infection, HDV prevalence is generally low among both asymptomatic HBV carriers (<10%) and among patients with chronic HBV-related liver disease (<25%). HDV infection in these countries occurs most commonly among injecting drug users and persons with hemophilia. In countries with moderate and high levels of chronic HBV prevalence, the prevalence of HDV infection is highly variable. In southern Italy and in parts of Russia and Romania, the prevalence of HDV infection is very high among both asymptomatic HBV carriers (>20%) and among patients with HBV-related chronic liver disease HBV (>60%). Other countries, including northern Italy, Spain, Turkey, and Egypt, have a moderate prevalence of HDV infection among asymptomatic HBV carriers (10%–19%) and among patients with chronic HBV-



related liver disease (30%–50%). However, in most of Southeast Asia and China, where the prevalence of chronic HBV infection is very high, HDV infection is uncommon. In some South American countries in the Amazon River Basin, periodic epidemics of HDV infection have occurred among chronic HBV carriers in relatively isolated regions. Disease related to HDV infection in these outbreaks has been very severe, with rapid progression to fulminant hepatitis and case-fatality rates of 10%–20%. The cause of the atypical course of HDV infection in these populations is unknown.

## ✓ PUBLIC HEALTH CONTROL MEASURES

### Public Health Responsibility

- Investigate suspect cases of disease for the following groups and enter data into UT-NEDSS:
  - Women of childbearing age (12–50 years of age)
  - Co-infected individuals (with hepatitis C, D or HIV/AIDS)
  - Suspected acute cases.
- Provide education to the general public and clinicians regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.
- Identify sources of exposure and stop further transmission.
- Ensure identification of infected pregnant women, and prevent perinatal transmission to their babies.
- Collect surveillance data in order to assess groups and areas where public health intervention may be needed.

### Prevention

Persons with acute or chronic HBV and/or HDV infections should prevent their blood and other potentially infective body fluids from contacting other persons. They should not donate blood or share toothbrushes or razors with household members. Testing all pregnant women for HBsAg is recommended because measures can be implemented to prevent spread from infected mothers to their infants. Donated blood should be tested for HBsAg, and rejected if positive. Syringes, acupuncture and tattooing needles should never be reused. Household contacts of infected persons should be vaccinated. Vaccination is highly effective in preventing HBV infection. Since HDV cannot be transmitted in the absence of HBV infection, the prevention of HBV infection through immunization is the best way to prevent HDV infection. However, no products exist to prevent HDV super-infection of persons with chronic HBV infection. Thus, prevention of HDV super-infection depends primarily on education to reduce risk behaviors.

\*Any blood spills, including dried blood, which can still be infectious, should be cleaned using 1:10 dilution of one part household bleach to 10 parts of water for disinfecting the area. Gloves should be used when cleaning up any blood spills.

## Post-Exposure Prophylaxis

When indicated, hepatitis B immune globulin (HBIG) should be given as soon after exposure as possible. HBV vaccine is also recommended for people at high risk of additional exposure. Depending on the exposure circumstance, the HBV vaccine series may be started at the same time as treatment with HBIG. For infants born to infected mothers, the combination of HBIG and vaccine is effective at preventing infection. HBV vaccination and one dose of HBIG administered within 24 hours after birth are 85–95% effective in preventing both acute HBV infection and chronic infection in the infant. Vaccination against HBV will prevent HDV co-infection.

## Vaccine

Two single antigen (e.g., monovalent) recombinant HBV vaccines, are available for use in the U.S.: Engerix-B and Recombivax HB. These vaccines are supplied in different concentrations and have different doses. They can be used interchangeably, except that only Recombivax HB can be used for the 2-dose series in adolescents age 11–15 years.

In addition, recombinant hepatitis B vaccine is a component in two combination vaccines, which can be used if the child or adolescent is due for the other vaccine components:

- Pediarix – Diphtheria and tetanus toxoids and acellular pertussis (DTaP), hepatitis B (Engerix-B 10 mcg/mL), and inactivated poliovirus vaccine (IPV), are typically administered at two, four, and six months of age; the DTaP-HepB-IPV combination vaccine should **not** be administered before six weeks or after seven years of age.
- Twinrix – Hepatitis A and hepatitis B (Engerix-B 20 mcg); this vaccine is approved for individuals ≥18 years of age.

In February 2018, the Advisory Committee on Immunization Practices (ACIP) approved recommendations for Heplisav-B (HepB-CpG) vaccine as an option for previously unvaccinated or incompletely vaccinated persons, including:

- Adults 18 years of age or older who have a specific risk, or lack a risk factor, but want protection. See [ACIP Recommended Immunization Schedule for Adults](#) for risk factors.

### Recommendations for administering Heplisav-B vaccine

- Screen for contradictions and precautions. Do not administer Heplisav-B to individuals with a history of severe allergic reaction after a previous dose of any hepatitis B vaccine or to any component of Heplisav-B, including yeast.
- Schedule: Administer 2 doses at least 4 weeks apart
- Dose (volume): 0.5 mL each dose
- Route: Intramuscular (IM) injection
- Site: Deltoid muscle is preferred
  - Identify the site carefully using anatomical landmarks. Shoulder injury related to vaccine administration (SIRVA) has been reported after IM injections in the deltoid muscle.
- See [Vaccine Administration](#) and [SIRVA infographic](#) for more information about proper IM vaccine administration.

## Interchangeability and Dosing Schedule

- 2-dose HepB vaccine series only applies when both doses consist of HepB-CpG, administered at least 4 weeks apart.
- Series consisting of a combination of 1 dose of HepB-CpG and a vaccine from a different manufacturer (HepB-alum) should do the following:
  - Adhere to the 3-dose schedule, with minimum intervals of 4 weeks between dose 1 and 2, 8 weeks between dose 2 and 3, and 16 weeks between dose 1 and 3. However, if HepB-CpG is substituted for dose 2 of HepB-alum, a provider has the option of administering the next dose of HepB-CpG a minimum of 4 weeks from the previous dose for a complete series.
- Doses administered at less than the recommended minimum interval should be repeated.
- See [Recommended Immunization Schedule for Adults](#) for details.

## Special Populations

- Until safety data are available for HepB-CpG, providers should continue to vaccinate pregnant women needing HepB vaccination with HepB-alum.
- Post-vaccination serologic testing 1–2 months after the final dose of vaccine is recommended for certain persons, including those who are immunocompromised and health care personnel.

Another combination vaccine (Comvax), which contained HBV vaccine and *H. influenzae* type b conjugate vaccine, was discontinued in 2014. Hepatitis B vaccines are administered intramuscularly (IM). HBV vaccines administered by any route other than IM should not be counted as valid and should be repeated. Hepatitis B vaccines should be refrigerated at a temperature between 36°F and 46°F (2°C and 8°C). Dosing requirements are shown in the table below:

**Table 2. Hepatitis B vaccine dosing requirements**

Age Group	Single-Antigen Vaccine				Combination Vaccine			
	Recombinax HB		Engerix-B		Pediatrix		Twinrix	
	Dose HBaAG, mcg	Volume, mL	Dose HBaAG, mcg	Volume, mL	Dose HBaAG, mcg	Volume, mL	Dose HBaAG, mcg	Volume, mL
<6 weeks	5	0.5	10	0.5	NA	NA	NA	NA
6 weeks to 7 years	5	0.5	10	0.5	10	0.5	NA	NA
7 to 10 years	5	0.5	10	0.5	NA	NA	NA	NA
11 to 15 years	10*	1	NA	NA	NA	NA	NA	NA
	5	0.5	10	0.5	NA	NA	NA	NA
16 to 18 years	5	0.5	10	0.5	NA	NA	NA	NA
18 years	5	0.5	10	0.5	NA	NA	20	1
≥20 years	10	1	20	1	NA	NA	20	1
<b>Hemodialysis patients and other immunocompromised persons</b>								
<20 years	5	0.5	10	0.5	NA	NA	NA	NA
≥20 years	40^	1	40	2~	NA	NA	NA	NA

\*Adult formulation administered on a 2-dose schedule at 0 and 4 to 6 months.

^Dialysis formulation administered on a 3-dose schedule at 0, 1, and 6 months.

~Two 1-mL doses administered at one site, on a 4-dose schedule at 0, 1, 2, and 6 months.

The HBV vaccine is both safe and effective. After three intramuscular doses of HBV vaccine, more than 90% of healthy adults and more than 95% of infants, children, and adolescents (from birth to 19 years of age) develop adequate antibody responses. The vaccine is 80–100% effective in preventing infection or clinical hepatitis in those who receive the complete course of vaccine. Immune memory remains intact for more than 15 years following immunization, and both adults and children with declining antibody levels are still protected against significant HBV infection. Chronic HBV infection has only rarely been documented among vaccine responders.

HDV is prevented by routine HBV vaccination. Apart from the morbidity and mortality associated with HBV infection, these individuals are at risk of HDV infection. Thus, every effort should be made to reduce the risk of HDV transmission to HBV carriers.

### **Routine infant vaccination**

HBV vaccination is recommended for all infants. The first dose should be given shortly after birth and before hospital discharge. The second dose should be given at 1–2 months, with the third dose given at 6–18 months. Combination vaccines that include HBV are also available. The hepatitis B-DTaP-IPV combination (Pediatrix) should be given on the same schedule as the HBV vaccination. The hepatitis B-Hib combination (Comvax) was previously given at 2, 4, and 12 through 15 months of age, but was discontinued in 2014.

### **Routine childhood and adolescent vaccination**

Routine HBV vaccination is also recommended for all children and adolescents through age 18 years of age. Three doses should be administered. The first two doses should be separated by no less than four weeks, and a third dose 4–6 months after the second dose. A combination hepatitis A/B vaccine (Twinrix) is available for persons 18 years and older. Three doses of the hepatitis A/B vaccine should be administered, on the same schedule as the HBV vaccinations. A 4-dose accelerated hepatitis A/B vaccination schedule is also approved, with doses given at 0, 7, and 21 through 30 days and a booster dose 12 months after the first dose.

### **Adults at high risk**

Vaccination is also recommended for adults at increased risk of HBV infection. The schedule for adults should follow that for children and adolescents. Adults considered at increased risk for HBV infection include:

- Men who have sex with other men
- Heterosexuals with multiple sex partners
- Persons diagnosed with a recently acquired sexually transmitted disease
- Prostitutes
- Injection-drug users who share needles
- Inmates of long-term correctional facilities
- Persons undergoing hemodialysis
- Healthcare workers (depends on how often they are exposed to blood or blood products through percutaneous and permucosal exposures).

### **Other populations**

Vaccination should also be considered for:

- Clients and staff of institutions for the developmentally disabled

- Household members and sex partners of HBV carriers
- Adults and children who plan to travel to areas outside the U.S.
- Recipients of certain blood products, such as persons with hemophilia, who are at high risk of infection.
- Pregnant women who are identified as being at risk for HBV infection during pregnancy – pregnancy is *not* a contraindication to vaccination.
- Individuals with diabetes, as recommended by the ACIP in December 2011 should be considered for the vaccine under the following recommendations:
  - HBV vaccination should be administered to unvaccinated adults with diabetes mellitus who are aged 19 through 59 years (recommendation category A; evidence type 2).
  - HBV vaccination may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes mellitus who are aged ≥60 years (recommendation category B; evidence type 2).

### **Pre-vaccination serologic testing**

Pre-vaccination serologic testing is not indicated before routine vaccination of children or adolescents. Pre-vaccination testing is recommended for:

- Foreign-born persons from endemic countries
- Children of immigrants from endemic countries
- Unvaccinated household, sexual, and needle-sharing contacts of HBV carriers
- HIV-infected persons.

Pre-vaccination testing should be considered for:

- Men who have sex with men
- Injection-drug users
- Incarcerated persons.

### **Post-vaccination serologic testing**

Post-vaccination serologic testing is not routinely recommended for most infants, children, adolescents, and adults. It should, however, be considered for persons whose subsequent management depends on knowing their immune status, including:

- Infants born to HBsAg-positive women
- Chronic hemodialysis patients
- Immunocompromised persons
- Persons with HIV
- Healthcare workers who have significant exposure to HBV
- Sex partners of HBsAg-positive persons.

Post-vaccination testing should be performed 1–2 months after completion of the vaccine series. Children born to HBsAg-positive women should be tested at 9–18 months. Healthcare workers who have contact with patients or blood and are at ongoing risk for injuries with sharp instruments or needle sticks should be routinely tested for antibody after vaccination.

### **Management of non-response to hepatitis B vaccine**

The current recommendation for all healthy individuals who do not develop an adequate anti-HBs response to the primary vaccine series is to administer one or more additional doses. An adequate antibody response is seen in 15–25% after one additional dose and in 50% after three additional doses. As a result, it may be reasonable to repeat a 3-dose schedule, retesting two to three months after the third dose. Individuals who fail to respond after three additional doses of vaccine that have been appropriately administered are unlikely to benefit from further vaccination. However, these individuals may still mount an adequate immune response and recover from HBV infection.

Individuals who fail to respond after two courses of HBV vaccine should be tested for HBsAg, particularly in countries where pre-vaccination testing is not performed or performed using anti-HBs test only. Non-responders who test negative for HBsAg should be educated on how to prevent HBV infection, including the need for hepatitis B immune globulin (HBIG) if they have an exposure to blood or other body fluids of a person who is HBsAg-positive.

### **Booster doses**

Booster doses are not recommended for persons with a normal immune status who were vaccinated as infants, children, or adolescents. However, booster doses are recommended for hemodialysis patients, if annual testing of anti-HBs levels decline to <10 mIU/mL.

For other immunocompromised persons (e.g., HIV-infected persons, hematopoietic stem cell transplant recipients, and persons receiving chemotherapy), the need for booster doses has not been determined. Annual anti-HBs testing and booster doses when anti-HBs levels decline to <10 mIU/mL should be considered in persons with an ongoing high risk for exposure.

### **Interruption in schedule**

There are no maximum intervals, and it is not necessary to restart the series of any vaccine due to extended intervals between doses.

### **\*Sound-alike/look-alike issues**

- Engerix-B adult may be confused with Engerix-B pediatric/adolescent.
- Recombivax HB may be confused with Comvax.
- Recombivax HB may be confused with Recombivax HB Dialysis Formulation.

## **Isolation and Quarantine Requirements**

**Isolation:** Staff and students ill with acute HBV and/or acute HDV should stay home until they feel well and until fever and jaundice are gone. Otherwise, no isolation measures are necessary.

**Hospital:** NA

**Quarantine:** NA



## CASE INVESTIGATION

### Reporting

All forms of HBV infection should be reported to the Utah Department of Health. Report any illness to the Utah Department of Health that meets any of the following criteria:

#### Acute hepatitis B infections

##### Clinical case definition

###### *Clinical evidence*

An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain), and either a) jaundice, or b) elevated serum alanine aminotransferase (ALT) levels >100 IU/L.

\*A documented negative HBsAg laboratory test result within six months prior to a positive test (either HBsAg, HBeAg, or HBV NAT, including genotype) result does not require an acute clinical presentation to meet the surveillance case definition.

##### Laboratory criteria for diagnosis

- Hepatitis B surface antigen (HBsAg) positive **AND**
- IgM antibody to hepatitis B core antigen (IgM anti-HBc) positive (if done).

##### Case classification

###### *Confirmed*

A case that meets the clinical case definition is laboratory confirmed, and is not known to have chronic HBV infection.

##### Administrative data

A person whose death certificate lists acute HBV infection as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures:

- All cases of acute HBV infection should be reported.
- Reporting should be ongoing and routine.
- Frequency of reporting should follow the routine schedule of the Utah Department of Health.

**Table 3. Criteria for reporting acute hepatitis B (CTSE 2012)**

Criterion	Reporting				
Clinical Evidence					
Jaundice		N		N	
Acute onset		N	N	N	N
Fever		O	O	O	O
Headache		O	O	O	O
Malaise		O	O	O	O

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Anorexia		O	O	O	O
Nausea		O	O	O	O
Vomiting		O	O	O	O
Diarrhea		O	O	O	O
Abdominal pain		O	O	O	O
<i>Clinical and Administrative Data</i>					
Healthcare record contains a diagnosis of acute hepatitis B	S				
Death certificate lists acute hepatitis B as a cause of death or a significant condition contributing to death	S				
<i>Laboratory Evidence</i>					
Elevated serum aminotransferase (ALT) or (AST) levels			N		N
IgM antibody to hepatitis B core antigen (IgM anti-HBc) positive	S	N	N		
Hepatitis B surface antigen (HBsAg) positive	S			N	N

Notes:

S = This criterion alone is sufficient to report a case

N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to report a case.

O = At least one of these “O” criteria in each category in the same column (e.g., clinical presentation and laboratory findings)—in conjunction with all other “N” criteria in the same column—is required to report a case.

**Chronic hepatitis B infections**

- 1) Any person with a positive result for any one of the following three laboratory tests:
  - Hepatitis B surface antigen (HBsAg),
  - Hepatitis B e antigen (HBeAg) or
  - Nucleic acid test for HBV-DNA (including qualitative, quantitative and genotype testing).
- 2) A person whose healthcare record contains a diagnosis of chronic HBV.
- 3) A person whose death certificate lists chronic HBV as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures:

- All cases of chronic HBV should be reported.
- Reporting should be ongoing and routine.
- Frequency of reporting should follow the routine schedule of Utah Department of Health.



**Table 4. Criteria for reporting chronic hepatitis B (CTSE 2012)**

Criterion	Reporting
<i>Clinical and Administrative Data</i>	
Healthcare record contains a diagnosis of disease due to chronic hepatitis B	S
Death certificate lists disease due to chronic hepatitis B as a cause of death or a significant condition contributing to death	S
<i>Laboratory Evidence</i>	
Hepatitis B surface antigen (HBsAg) positive	S
Hepatitis B e antigen (HbeAg) positive	S
Nucleic acid test for hepatitis b virus DNA (HBV-DNA) positive	S

Notes:

S = This criterion alone is sufficient to report a case.

**Table 5. Criteria for reporting perinatal hepatitis B (CSTE 2016)**

Criterion	Maternal	Maternal	Infant/Child	Infant/Child	Infant
<i>Clinical Evidence</i>					
Diagnosis of hepatitis B infection		N		O	
Pregnant	N	N			
Born to a woman with evidence of hepatitis B infection (HBsAg), HBeAg, or HBV-DNA positive, or diagnosis of hepatitis B infection					O
Maternal HBsAg status unknown at time of hospital discharge					O
<i>Laboratory Evidence</i>					
HBsAg positive	O		O		
HBeAg positive	O		O		
HBV-DNA positive	O		O		
<i>Demographic</i>					
24 months of age or younger			N	N	
Newborn					N

Notes:

S = This criterion alone is Sufficient to report a case.

N = All "N" criteria in the same column are Necessary to report a case.

O = At least one of these "O" (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column- in conjunction with all "N" criteria in the same column – is required to report a case.

\*A requisition or order for any of the "S" laboratory tests is Sufficient to meet the reporting criteria.

For purposes of perinatal HBV surveillance, maternal and infant status should be ascertained.

### **Pregnant women**

All pregnant women should be tested for HBsAg during each pregnancy as part of routine prenatal care. All HBV-infected women must be reported to the state or local public health authority as mandated by law or regulation.

Report pregnancy status along with test results for women to public health authorities who meet any of the following criteria:

Positive result for any one of the following three laboratory tests:

- hepatitis B surface antigen (HBsAg)
- hepatitis B e antigen (HBeAg)
- nucleic acid test for HBV-DNA (including qualitative, quantitative and genotype testing).

Immediately determine HBsAg status on all pregnant women presenting for labor and delivery without documentation of HBsAg test results for current pregnancy and those with risk factors regardless of previous HBsAg test results.

Other recommended reporting procedures:

- All cases of chronic HBV should be reported.
- All cases of HBV should be reported with sex and age accurately documented and should include pregnancy status, if known.
- Reporting should be ongoing and routine.

### **Infants**

Report all infants delivered to women who are HBsAg positive or HBsAg status unknown to the health authority.

Report all infants with evidence of HBV infection as evidenced by the following laboratory tests: HBsAg, hepatitis B nucleic acid (HBV DNA), or hepatitis B e antigen (HBeAg).

## **Disease-Specific Data Elements**

### **Maternal**

- Country of birth
- Race
- Ethnicity
- Date of birth
- HBsAg – result, date
- HBeAg result, date
- HBV DNA (or genotype), result, date
- Alanine aminotransferase (ALT)
- Maternal antiviral therapy, if any (Yes/No/Unknown)
- Coinfection with human immunodeficiency virus or HCV
- State/Territory of residence at time of infant's diagnosis

## **Infant**

- HBsAg, HBeAg and HBV DNA test results and date of test performance
- Anti-HBs test results and date of test performance
- HBIG administration -time and date
- HBV vaccine birth dose time and date, dates of other valid HBV vaccine doses
- Birthweight
- Date of birth
- Time of birth (military time)
- State/Territory of birth
- State/Territory of residence at time of diagnosis

## **Case Definition**

### **Hepatitis B, acute (2012)**

#### **Clinical case definition**

##### *Clinical evidence*

An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain), and either a) jaundice, or b) elevated serum alanine aminotransferase (ALT) levels >100 IU/L.

\*A documented negative HBsAg laboratory test result within six months prior to a positive test (either HBsAg, HBeAg, or HBV NAT, including genotype) result does not require an acute clinical presentation to meet the surveillance case definition.

#### **Laboratory criteria for diagnosis**

- Hepatitis B surface antigen (HBsAg) positive **AND**
- IgM antibody to hepatitis B core antigen (IgM anti-HBc) positive (if done).

#### **Case classification**

##### *Confirmed*

A case that meets the clinical case definition is laboratory confirmed, and is not known to have chronic HBV infection.

**Table 6. Criteria for classification of acute hepatitis B (CSTE 2012)**

	Case Definition		
Criterion	Confirmed		
<i>Clinical Presentation</i>			
Jaundice	N		
Acute onset of symptoms	N	N	
Fever	O	O	
Headache	O	O	
Malaise	O	O	
Anorexia	O	O	
Nausea	O	O	
Vomiting	O	O	
Diarrhea	O	O	
Abdominal pain	O	O	
<i>Laboratory Findings</i>			
Elevated serum aminotransferase (ALT) levels >100IU/L		N	
IgM antibody to hepatitis B core antigen (anti-HBc) positive (if done)	N	N	
Hepatitis B surface antigen (HBsAg) positive	N	N	O
Hepatitis B e antigen (HBeAg) positive			O
Hepatitis B DNA (HBV-DNA) positive			O
Negative HBsAg within 6 months prior to a positive test			N
<i>Clinical Evidence</i>			
No previous diagnosis of chronic hepatitis B	N	N	N

Notes:

N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to classify a case.

O = At least one of these “O” criteria in each category in the same column (e.g., clinical presentation and laboratory findings)—in conjunction with all other “N” criteria in the same column—is required to classify a case.

## Hepatitis B, chronic (2012)

### Clinical description

#### *Clinical evidence*

No symptoms are required. Persons with chronic HBV infection may have no evidence of liver disease or may have a spectrum of disease ranging from chronic hepatitis to cirrhosis or liver cancer.

### Laboratory criteria

- IgM antibodies to hepatitis B core antigen (IgM anti-HBc) negative AND a positive result on one of the following tests: hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), or nucleic acid test for HBV-DNA (including qualitative, quantitative and genotype testing) **OR**
- HBsAg positive or nucleic acid test for HBV-DNA positive (including qualitative, quantitative and genotype testing) or HBeAg positive two times at least six months apart (Any combination of these tests performed 6 months apart is acceptable).

### Case classification

#### Confirmed

A person who meets either of the above laboratory criteria for diagnosis.

#### Probable

A person with a single HBsAg positive or HBV-DNA positive (including qualitative, quantitative and genotype testing) or HBeAg positive lab result and does not meet the case definition for acute hepatitis B.

#### Comment

Multiple laboratory tests indicative of chronic HBV infection may be performed simultaneously on the same patient specimen as part of a “hepatitis panel.” Testing performed in this manner may lead to seemingly discordant results, e.g., HBsAg-negative AND HBV-DNA-positive. For the purposes of this case definition, any positive result among the three laboratory tests mentioned above is acceptable, regardless of other testing results. Negative HBeAg results and HBV-DNA levels below positive cutoff level do not confirm the absence of HBV infection.

**Table 7. Criteria for classification of chronic hepatitis B (CSTE 2012)**

	Case Definition		
Criterion	Confirmed		Probable
Laboratory Evidence			
Hepatitis B surface antigen (HBsAg) positive	O <sup>1</sup>	O <sup>2</sup>	O <sup>1</sup>
Hepatitis B e antigen (HBeAg) positive	O <sup>1</sup>	O <sup>2</sup>	O <sup>1</sup>
Nucleic acid test for hepatitis B virus (HBV) DNA positive	O <sup>1</sup>	O <sup>2</sup>	O <sup>1</sup>
Hepatitis B core antigen (anti-HBc) IgM negative	N		
Does not meet acute hepatitis B definition			O

Notes:

N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to classify a case.

O = At least one of these “O” criteria in each category in the same column—in conjunction with all other “N” criteria in the same column—is required to classify a case.

Laboratory finding labeled O<sup>1</sup> are a single specimen.

Laboratory findings labeled O<sup>2</sup> are two positive specimens spaced at least six months apart. The O<sup>2</sup> laboratory tests may be used in any combination, so long as there is a minimum interval of six months between specimens.

## **Hepatitis B, perinatal (2016)**

### **Clinical description**

Perinatal HBV infection in a child  $\leq 24$  months of age may range from asymptomatic to fulminant hepatitis.

### **Laboratory criteria**

Laboratory evidence of HBV infection in a child consists of one or more of the following:

- positive HBsAg test (only if at least four weeks after last dose of HBV vaccine)
- positive HBeAg test, or
- detectable HBV DNA.

### **Epidemiologic linkage**

Born to a HBV-infected mother.

### **Case classification**

#### *Confirmed*

A child born in the U.S. to a HBV-infected mother and positive for HBsAg at  $\geq 1$  month of age and  $\leq 24$  months of age OR positive for HBeAg or HBV DNA  $\geq 9$  months of age and  $\leq 24$  months of age.

#### *Probable*

A child born in the U.S. and positive for HBsAg at  $\geq 1$  month of age and  $\leq 24$  months of age OR positive for HBeAg or HBV DNA  $\geq 9$  months of age and  $\leq 24$  months of age, but whose mother's HBV status is unknown (e.g., epidemiologic linkage not present).

#### *Comment*

Infants born to HBV-infected mothers should receive HBIG and the first dose of HBV vaccine within 12 hours of birth, followed by the second and third doses of HBV vaccine at one and six months of age, respectively. PVST for HBsAg and anti-HBsAg is recommended one to two months following completion of the vaccine series, but not earlier than nine months of age.

If mother known to not be infected with HBV, refer to the case definition for acute HBV.

**Table 8. Criteria for classification of perinatal hepatitis B (CSTE 2016)**

Criterion	Probable			Confirmed		
<i>Demographic</i>						
Age $\geq 1$ and $< 9$ months	O			O		
Age $\geq 9$ and $\leq 24$ months	O	N	N	O	N	N
Born in the U.S.	N	N	N	N	N	N
<i>Laboratory Evidence</i>						
HBsAg positive	N			N		
HBeAg positive		N			N	
Detectable HBV-DNA			N			N
$\geq 4$ weeks since last dose of HBV vaccine	N			N		
<i>Epidemiological Evidence</i>						
Maternal HBV infection				N	N	N
HVB status of mother unknown	N	N	N			

Notes:

N = All “N” criteria in the same column are Necessary to classify a case. A number following an “N” indicates that this criterion is only required for a specific subtype (see below). If the absence of a criterion (e.g., criterion NOT present) is required for the case to meet the classification criteria, list the Absence of criterion as a Necessary component.

O = At least one of these “O” (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column – in conjunction with all “N” criteria in the same column – is required to classify a case. (These “O” criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.) A number following an “O” indicates that this criterion is only required for a specific disease/condition subtype.

## Hepatitis D, co-infection

### Clinical case definition

No clinical case definition is available.

### Laboratory criteria

- IgM antibody to hepatitis D (anti-HDV) positive **AND**
- IgM antibody to hepatitis B core antigen (anti-HBc) positive.

### Case classification

#### *Confirmed*

A case that meets the clinical case definition and is laboratory confirmed.

## Hepatitis D, super-infection

### Clinical case definition

No clinical case definition is available.

### Laboratory criteria

- IgM antibody to hepatitis D (anti-HDV) positive **AND**
- IgM antibody to hepatitis B core antigen (anti-HBc) negative.

## **Case classification**

### *Confirmed*

A case that meets the clinical case definition and is laboratory confirmed.

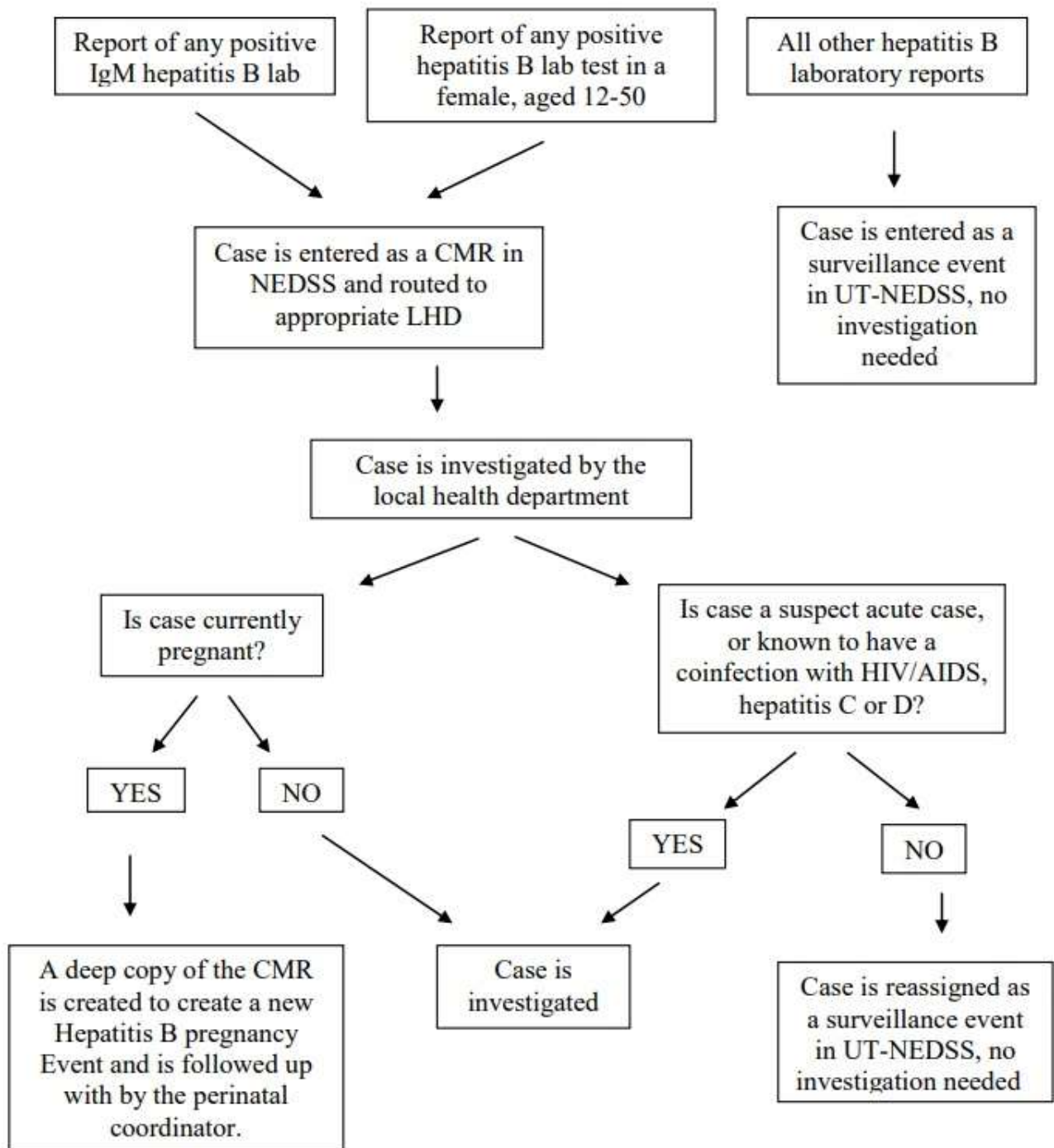
## **Case Investigation Process**

- Enter a confidential morbidity report (CMR) into UT-NEDSS as a 'Hepatitis B, Chronic' (investigation will determine if this needs to be changed later to an acute case classification).
- The following groups are to be investigated when a positive HBV lab report or report of disease is given to public health:
  - Suspect acute cases
  - Individuals who are co-infected with one of the following: hepatitis C, hepatitis D, HIV or AIDS.
  - Women of child bearing age (12–50 years of age)
    - Women who are found to be pregnant should have a new CMR created in UT-NEDSS through a deep copy of the existing record and classified as a 'Hepatitis B Pregnancy Event' for perinatal case management and follow-up.
- Although rare, the following should also be investigated:
  - Infants born to HBsAg positive mothers who were not given prenatal care and/or no vaccine was administered to the infant.
  - Mothers with unknown HBsAg status, whose infant has been reported as receiving HBIG within seven days of birth
    - Mother would be investigated as a pregnancy event.
- Assure that all case contacts of the above investigated groups are identified and appropriately managed.



## Hepatitis B Case Investigation Process for Local Health Jurisdictions

All cases/positive laboratory results reported to public health will follow the following algorithm:



## **Outbreaks**

HBV and HDV do not typically cause outbreaks. When two or more cases occur in association with some common exposure, search for additional cases. Consider vaccination of susceptible persons at risk for exposure.

Information on the investigation and management of HBV or HDV outbreaks in particular settings can be found at <http://www.cdc.gov/hepatitis/Settings>.

## **Identifying Case Contacts**

Close contacts of persons diagnosed with HBV and/or HDV are household members and sex partners. Transmission of HBV in schools and childcare settings is most likely to occur through direct exposure to blood after an injury or from bites or scratches that break the skin and introduce blood or body secretions from an HBV carrier into another person. The risk of transmission of HBV and/or HDV in the school and childcare setting has always been low, and with universal vaccination, exposure in the school setting does not require contact notification. Currently there are no recommendations by CDC or the Committee on Infectious Disease (authors of the Red Book) to implement contact investigations in school or child care settings. Universal precautions should be followed by staff.

## **Case Contact Management**

### **Infants born to HBsAg-positive mothers**

- Newborns born to HBsAg-positive mothers should receive HBIG (0.5 mL IM) and the first dose of HBV vaccine within 12 hours of birth. The vaccination schedule is dependent on weight at birth.
  - Infants born that weigh  $\geq 2000$  grams should receive a 3-dose vaccination series with doses administered at 0, 1–2, and 6 months of age.
  - Infants born that weight  $< 2000$  grams should receive a 4-dose vaccination series with doses administered at 0, 1–2, 2–3, and 6–7 months of age.
  - Hepatitis B-containing combination vaccines may be used for perinatal children, but not as a birth dose. Perinatal children receiving combination vaccines should have a HBV birth dose, then transition to the combination vaccine.
- The infant should be screened for HBsAg and anti-HBs after completion of the immunization series at 9–15 months of age, to monitor the success or failure of the immunization. Testing should not be performed before nine months of age to avoid detection of anti-HBs from HBIG administered during infancy and to maximize the likelihood of detecting HBV infections. If HBsAg is not present and anti-HBs antibody is  $\geq 10$  mIU/mL, children can be considered protected.
- Infants with anti-HBs concentrations of  $< 10$  mIU/mL and who are HBsAg-negative should receive three additional doses of vaccine in a 0, 1, and 6-month schedule, followed by testing for anti-HBs 1–2 months after the sixth dose. No data suggest that children who have no detectable antibody after six doses of vaccine would benefit from any additional doses.
- Infants who become HBsAg-positive despite immunization (because of intrauterine infection or vaccine failure) should be referred to a pediatric hepatologist for follow-up, and the parents should be counseled.

**Infants born to mothers whose HBsAg status is unknown**

- Newborns born to mothers whose HBsAg status is not known should be given HBV vaccine within 12 hours of birth while awaiting HBsAg test results on the mother.
- If the mother is determined to be positive, the infant should receive HBIG as soon as possible, within seven days of birth. This child should then complete the 3-dose HBV vaccination series according to birth weight. The child should then be screened for HBsAg and anti-HBs at 9–18 months of age.
- If the mother is determined to be HBsAg-negative, the infant should complete the 3-dose HBV vaccine series according to the schedule for infants born to HBsAg-negative mothers (0, 1–2, 6–18 months).
- If the mother's HBsAg status remains unknown, the infant should complete the vaccine series according to the recommended schedule for infants born to HBsAg-positive mothers (0, 1–2, 6 months). Administration of HBIG is not necessary.

**Infants exposed after birth**

- Children younger than 12 months of age who have close contact with primary caregivers with acute infection require immunoprophylaxis.
- If at the time of exposure, the infant has been fully immunized or has received at least two doses of vaccine, the infant should be presumed protected, and HBIG is not required.
- If only one dose of vaccine has been administered, the second dose should be administered if the interval is appropriate, or HBIG should be administered if immunization is not due.
- If immunization has not been initiated, the infant should receive HBIG (0.5 mL) and should initiate and complete the 3-dose HBV vaccine series.

**Sexual exposure to HBV infection**

- Sexual contacts of a person with HBV who is under investigation (women of childbearing age, suspect acute cases and co-infected individuals) if susceptible, should begin the hepatitis B vaccine series.
  - Contacts who are insured by a health insurance plan should use that for vaccine coverage.
  - For uninsured adult contacts, LHDs or private providers can offer vaccine purchased privately or publicly (as available) and bill according to established billing policies.
  - For children contacts <18 years of age, vaccine is available through the Vaccines for Children (VFC) Program for children who are eligible for that program. Uninsured children would have access to VFC vaccine, but parents would be required to pay the administration fee to the provider.
- Pre-vaccination serologic testing can determine if the sexual contact is susceptible to HBV.
- If the sexual exposure is to a person with acute HBV infection, then the contact should receive a single dose of HBIG (0.06 mL/kg) with the first vaccine dose.
- HBIG administration is unlikely to be beneficial if given more than 14 days after exposure.

**Household/close contact exposure to HBV infection**

- All susceptible household contacts, including infants, of persons who are under investigation (women of childbearing age, suspect acute cases and co-infected individuals) with HBV should initiate and complete the 3-dose series of HBV vaccine according to age specifications.

- Contacts who are insured by a health insurance plan should use that for vaccine coverage.
- For uninsured adult contacts, LHDs or private providers can offer vaccine purchased privately or publicly (as available) and bill according to established billing policies.
- For children contacts <18 years of age, vaccine is available through the Vaccines for Children (VFC) Program for children who are eligible for that program. Uninsured children would have access to VFC vaccine, but parents would be required to pay the administration fee to the provider.
- Susceptible nonsexual household contacts of a person with acute HBV who have had a blood exposure to a case (such as sharing toothbrushes or razors) should receive a single dose of HBIG (0.06 mL/kg) with the first vaccine dose.

### **Percutaneous and mucosal exposure to HBV infection**

Appropriate post-exposure management depends on the HBsAg status of the source of the exposure and the hepatitis B vaccination status of the individual exposed.

#### **HBsAg-positive source**

- Unvaccinated persons or persons known not to have responded to a complete hepatitis B vaccine series should receive both HBIG and hepatitis B vaccine as soon as possible after exposure (preferably within 24 hours). The hepatitis B vaccine series should be completed using the age-appropriate vaccine dose and schedule.
- Persons who are in the process of being vaccinated but who have not completed the vaccine series should receive the appropriate dose of HBIG and should complete the vaccine series.
- Children and adolescents who have written documentation of a complete HBV vaccine series and who did not receive post-vaccination testing should receive a single vaccine booster dose.

#### **Source with unknown HBsAg status**

- Unvaccinated persons should begin the HBV vaccine series within 24 hours after exposure. The vaccine series should be completed using the age-appropriate dose and schedule.
- Persons who are not fully vaccinated should complete the vaccine series.
- Children and adolescents with written documentation of a complete HBV vaccine series require no further treatment.



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## **VERSION CONTROL**

Updated March 22, 2016: General update to formatting.

Updated March 25, 2016: Added the importance to public health section.

Updated March 25, 2016: Added reporting narrative and swimlanes.

Updated March 25, 2016: Added case classification swimlanes and updated to current CTSE guidelines.

Updated April 8, 2016: Added UT-NEDSS Minimum/Required fields.

Updated April 8, 2016: Reviewed and updated case fatality, reservoir, susceptibility, period of communicability, transmission, epidemiology, and incubation period.

Updated April 8, 2016: Added treatment information.

Updated April 8, 2016: Update to immunizations (\*Comvax discontinued in 2014).

Updated April 15, 2016: Update to serologic testing.

Updated April 15, 2016: Update to references.

Updated December 20, 2016: Added Perinatal HBV case classification and reporting swimlanes based on updated CSTE guidelines.

Updated May 1, 2018: Reviewed and verified disease updates.

Updated August 9, 2018: Added Critical Clinician Information.

Updated September 27, 2018: Reviewed and updated Minimum Data Set Requirements based on current case investigation form and message mapping guides, added Hepatitis B Rules for Entering Laboratory Test Results section.

Updated April 2019: Updated Critical Clinician Information, Laboratory Identification, Vaccine Information and Case Investigation Process.

Updated January 2022: Updated perinatal swimlane to match CSTE.



## UT-NEDSS MINIMUM/REQUIRED FIELDS BY TAB

### Demographic

- First name
- Last name
- Birth sex
- County
- Date of birth
- Country of birth
- Ethnicity
- Race
- State
- City
- Area code
- Zip code
- Street number
- Phone number

### Clinical

- Date diagnosed
- Date of death
- Died
- Disease
- Onset date
- Reason for testing
- Aware of hepatitis prior to lab testing?
- Pregnant; due date
- Jaundiced?
- Symptomology
- Does the patient also have hepatitis D?
- Does the patient have diabetes?
- Diagnosis date
- Acute onset
- History of vaccination for HBV?
- If vaccinated, how many doses has the patient received?
- Provider of care for hepatitis?
- Clinician first name
- Clinician last name
- Diagnostic facility (DF)
- DF City
- DF County
- DF State

### Laboratory

- ALT >100 IU/L
- Bilirubin >3.0 mg/dl
- Collection date
- Lab
- Organism
- Result value
- Test type
- Test result
- Negative HBV test in last 12 months?
- Test date
- Negative HBV test in last 6 months?
- Test date

### Investigation

- Prior to onset of symptoms or seroconversion, was patient hospitalized?
- Prior to onset of symptoms or seroconversion, was patient a resident of a LTCF?
- Ever inject drugs?
- Ever used street drugs, but not inject?
- Did the patient undergo hemodialysis?
- Did patient ever receive blood or blood products?
- Had a history of accidental stick or puncture with a contaminated sharps?
- Did patient receive blood or blood products?
- Did the patient receive any IV infusions and/or injections in an outpatient setting?
- Did the patient have other exposure to another person's blood?
- Was the patient employed in the medical or dental field having direct contact with blood?
- Was the patient employed as a public safety worker having contact with blood?
- Has patient ever had a tattoo?



- Has patient ever had a body piercing (other than ear)?
- Did the patient have dental work or oral surgery?
- History of surgery, other than oral
- Incarcerated longer than 24 hours?
- Type of facility
- Ever incarcerated longer than 6 months? Number of months & year of most recent incarceration
- Was patient ever treated for an STD? If yes, most recent year of treatment
- Contact of a confirmed or suspect case. If yes, type of contact (sexual, household (non-sexual), other)

- Number of female sex partners?
- Number of male sex partners?

### **Reporting**

- Date first reported to public health

### **Administrative**

- Outbreak name
- State case status
- Outbreak associated
- Infection Resolved?
- Resolved date

## ✓ HEPATITIS B RULES FOR ENTERING LABORATORY TEST RESULTS

The following rules describe how laboratory results reported to public health should be added to new or existing events in UT-NEDSS. These rules have been developed for the automated processing of electronic laboratory reports, although they apply to manual data entry, as well.

### Test-Specific Rules

*Test specific rules describe what test type and test result combinations are allowed to create new morbidity events in UT-NEDSS, and what test type and test result combinations are allowed to update existing events (morbidity or contact) in UT-NEDSS.*

Test Type	Test Result	Create a New Event	Update an Existing Event
Antigen by EIA/ELISA	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
Core Antibody (HBcAb)	Positive	No	Yes
	Negative	No	Yes
	Equivocal	No	Yes
	Other	No	Yes
E Antigen (HBeAg)	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
E Antibody (HBeAb)	Positive	No	Yes
	Negative	No	Yes
	Equivocal	No	Yes
Liver Function Tests (ALT, AST, bilirubin)	All	No	Yes
Genotype by PCR	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
PCR/Amplification	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
Surface Antibody (HBsAb)	Positive	No	Yes
	Negative	No	Yes
	Equivocal	No	Yes
	Other	No	Yes
Surface Antigen (HBsAg)	Positive	Yes	Yes
	Negative	No	Yes

**Hepatitis B (Chronic, Acute, Perinatal) and Hepatitis D: Utah Public Health Disease Investigation Plan**

	Equivocal	No	Yes
Surface Antigen (HBsAg) Confirmation	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
Total Antibody	Positive	No	Yes
	Negative	No	Yes
	Equivocal	No	Yes
Viral Load -- Quantitative	Positive	Yes	Yes
	Negative	No	Yes
	Other	No	Yes
Viral Load -- Qualitative	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes
Genotype by sequencing	Positive	Yes	Yes
	Negative	No	Yes
Pregnancy	Positive	No	Yes
	Negative	No	Yes
Core IgM Antibody*	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes

\*A positive result for this test would create a Hepatitis B, acute case.

## Whitelist Rules

*Whitelist rules describe how long an existing event can have new laboratory data appended to it. If a laboratory result falls outside the whitelist rules for an existing event, it should not be added to that event, and should be evaluated to determine if a new event (CMR) should be created.*

**Hepatitis B Morbidity Whitelist Rule:** Never a new case.

**Hepatitis B Contact Whitelist Rule:** If the specimen collection date of the laboratory result is six months or less after the event date of the contact event, the laboratory result should be added to the contact event.

**Liver Function Test Morbidity Whitelist Rule:** Never a new case.

**Liver Function Test Whitelist Rule:** Always added to contact.

## Graylist Rules

*We often receive laboratory results through ELR that cannot create cases, but can be useful if a case is created in the future. These laboratory results go to the graylist. The*

*graylist rule describes how long an existing event can have an old laboratory result appended to it.*

**Hepatitis B Graylist Rule:** If the specimen collection date of the laboratory result is 18 months before to seven days after the event date of the morbidity event, the laboratory result should be added to the morbidity event.

**Liver Function Test Graylist Rule:** If the specimen collection date of the laboratory result is 30 days before to seven days after the event date of the morbidity event, the laboratory result should be added to the morbidity event.

**Other Electronic Laboratory Processing Rules**

- If an existing event has a state case status of “not a case,” ELR will never add additional test results to that case. New labs will be evaluated to determine if a new CMR should be created.